Remarks

Upon entry of this Amendment, claims 20-25, 27-30, 32-39, 42 and 43 will be pending. Claims 40 and 41 have been withdrawn by the Examiner. Claim 26 has been cancelled, and claim 31 has been withdrawn without prejudice or disclaimer. Applicants reserve the right to prosecute the subject matter of the withdrawn and cancelled claims in a continuation, continuation-in-part or divisional application. Applicants have amended claims 20 and 25, currently on file, to more clearly define the scope of protection being sought. Support for the amendments can be found throughout the specification as filed, for example, at page 5, lines17-27; page 6, lines 1-4; page 8, lines 10-26; page 9, lines 8-17; and in the Examples. New claim 43 has been added. Support for the new claim can be found at, for example, at page 4, line 24 to page 5, line 2; page 9, lines 21-27; page 10, lines 13-15 and page 13, line 21 to page 14, line 1.

This Response is accompanied by a Declaration under 37 C.F.R. §1.132 by inventor Denis Leclerc (hereinafter referred to as the "Inventor's Declaration"), which provides evidence of the ability of a PapMV virus-like particle (VLP) to elicit a cellular immune response.

Information Disclosure Statement

The Examiner stated that the references indicated by strikethrough on the information disclosure statement attached to the Office Action were not considered because they either (i) failed to include a statement of the relevance of a non-English document, or (ii) failed to include a copy of a non-patent document.

Applicants are providing in the accompanying Supplemental Information Disclosure Statement copies of the non-patent documents indicated by strikethrough on the information disclosure statement attached to the Office Action, together with English translations of the abstract, or copies of the corresponding U.S. National Phase patent, for non-English documents indicated by strikethrough on the information disclosure statement attached to the Office Action.

35 U.S.C. 112, second paragraph

The Examiner rejected claims 20-39 and 42, under 35 U.S.C. 112 second paragraph, alleging the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The Examiner stated that claim 20 is drawn to a method for "potentiating an immune response..." and alleged that this language fails to define the scope of invention to one skilled in the art. In particular, the Examiner alleged that the skilled artisan would not understand whether claim 20 is drawn to inducing a cytokine response, a TH1 response, a TH2 response, an innate immune response, a mucosal immune response, or a systemic immune response.

Applicants respectfully traverse the Examiner's rejection. With respect to the threshold requirements of clarity and precision required under 35 U.S.C. 112, second paragraph, the MPEP clearly indicates at §2173.02: "The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of:
(A) The content of the particular application disclosure;
(B) The teachings of the prior art; and
(C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made."

Claim 20, currently on file, is directed to a method of "potentiating an immune response against an antigen" by administration of a defined adjuvant. Applicants assert that it is well known in the art, and also described in the "Background of the Invention" section of the instant application, that antigens are capable of eliciting various responses in a host, including for example humoral and cellular immune responses, which can be systemic or mucosal, and that adjuvants are commonly used to potentiate (or enhance) these responses. The instant specification at, for example, page 5, line 13 to page 6, line 4; page 6, lines 23-27; page 8, lines 10-27; page 9, lines 18-20, and in Examples II and III, provides additional description of the types of immunity (*e.g.* mucosal, humoral, cellular,

and innate) that may be potentiated by the administration of the PapMV-based adjuvant as claimed. As such, Applicants assert that a worker skilled in the art in light of the teachings of the instant application and common general knowledge at the time of filing would readily understand the meaning of the term "potentiating an immune response against an antigen" as recited in claim 20, currently on file, and, therefore, would fully understand the scope of the invention as claimed.

Applicants have, however, solely in order to expedite prosecution of the instant application, amended independent claim 20 to indicate that the immune response is a humoral and/or cellular immune response. Claim 31 has been withdrawn without prejudice or disclaimer. Applicants submit that the amended claim set submitted herewith complies with 35 U.S.C. 112, second paragraph, and, therefore, respectfully requests the withdrawal of this rejection.

35 U.S.C. 112, first paragraph (Enablement)

The Examiner rejected claims 20-31, 33-39 and 42, under 35 U.S.C. 112 first paragraph, alleging the claims fail to comply with the enablement requirement. The Examiner alleged that the claims contain subject matter which is not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention that is commensurate in scope with the claims without undue experimentation. The Examiner alleged that the specification only enables inducing a humoral immune response in a mammal and that the specification does not enable "potentiating an immune response" as claimed.

The Examiner stated that the language "potentiating an immune response" allows the claims to read on many different aspects of the mammalian immune response and that the state of the art at the time this application was filed would not allow the skilled artisan to predict whether a PapMV-based adjuvant would induce these types of immunity.

The Examiner further stated that the difficulty of these types of immunity claimed by the Applicants would require the skilled artisan to rely on the specification for reducing the invention to practice. The Examiner alleged, however, that the content of the specification only relates to using PapMV to induce TH2 (*i.e.* humoral) immunity and fails to provide adequate direction on how to regulate the types of immunity encompassed by the claims. Accordingly, the Examiner alleged that the skilled artisan would have to invest undue experimentation in order to practice the invention to induce the immune responses claimed.

Applicants respectfully traverse the Examiner's rejection. The test of enablement as defined in the MPEP at §2164.01 is "whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation" (*United States vs. Telectronics, Inc.*, 857 F.2d 778, 785, 8USPQ2d 1217, 1223 (Fed. Cir. 1988)) [emphasis added]. Independent claim 20, currently on file, is directed to a method of potentiating an immune response against an antigen by administering a PapMV, or PapMV VLP, adjuvant and the antigen to an animal. Applicants assert that the instant specification provides ample guidance with respect to how to make the PapMV, or PapMV VLP, adjuvant (see, for example, page 10, lines 1-15; page 11, lines 3-18; page 13, line 21 to page 14, line 21; and Examples I and III), and how to administer (*i.e.* use) the adjuvant together with an antigen (see page 11, lines 19-25, page 12, lines 7-15; page 13, lines 5-7; page 15, lines 5-11; and Example III). Moreover, methods of administering adjuvants and antigens to an animal in order to induce an immune response are well known to those skilled in the art. As such, Applicants assert that, a worker skilled in the art, having reference to the instant application, could readily practice the claimed method without undue experimentation.

With respect to the Examiner's comment pertaining to the types of immune response produced and their predictability, Applicants assert that a skilled worker would understand that, regardless of the immune response being potentiated, the method of

making and administering (*i.e.* using) the PapMV, or PapMV VLP, adjuvant would remain the same. Furthermore, Applicants submit that the teaching provided by the instant application, taken together with the knowledge in the art at the time of filing, provides a basis for sound prediction as to the ability of PapMV, or PapMV VLP, adjuvant to potentiate various types of immune responses. For example, the instant application, in addition to disclosing the acknowledged humoral response, demonstrates other properties of the PapMV VLPs including the ability to elicit a response on a systemic level (Examples II and III) and a TH1 response (Example II, at page 18), as well as teaching the use of PapMV and PapMV VLPs to potentiate cellular immunity (see, for example, page 5, line 13 to page 6, line 4, and page 8, lines 10-26). Moreover, it was well known in the art at the time the instant application was filed that adjuvants can augment various immune responses, including both humoral and cellular immune responses (see, for example, page 2, lines 1 to 8 of the specification) and that compounds or molecules, such as the *Salmonella typhii* porin protein described at page 22, lines 15-17 of the specification, which are capable of eliciting a humoral immune response are also capable of eliciting a cellular immune response. See also Brennan *et al.* (Molec. Biol. 2001 17:15-26, as cited by the Examiner at page 5 of the Office Action), at page 22 (Section 6), which indicates that the cowpea mosaic virus chimeras carrying the CTL epitope from lymphocytic choriomeningitis virus (LCMV) are capable of inducing CTL responses in addition to antibody production from B cells.

The teachings in the instant application are substantiated by the data provided in the accompanying Inventor's Declaration. This data shows that a recombinant PapMV coat protein (CP) produced by fusing the known pg33 CTL epitope (TSGGGKAVYNFATC-6H), a peptide derived from the surface glycoprotein of LCMV, to the C-terminus of the PapMV CP (as described in Example III of the instant specification with respect to the HCV epitopes) and administered to mice following standard protocols (as generally described at page 12, lines 7-15, and in Example II, of the instant application) is capable of inducing a cellular immune response.

Accordingly, Applicants assert that the instant application provides a basis for sound prediction that, contrary to the Examiner's allegation, the PapMV, or PapMV VLP, adjuvant can potentiate immune responses other than a humoral response, and that a skilled technician, having regard to the instant specification and the common general knowledge pertaining to the art of immunology, could readily practice the claimed method without undue experimentation. Moreover, Applicants respectfully remind the Examiner that patent applicants should not be required to limit their invention to specific examples. In *In re Goffe*, 542 F.2d 564, 567, 191 USPQ 429, 431 (CCPA 1976), the court stated: "[T]o provide effective incentives, claims must adequately protect inventors. To demand that the first to disclose shall limit his claims to what he has found will work or to materials which meet the guidelines specified for "preferred" materials in a process such as the one herein involved would not serve the constitutional purpose of promoting progress in the useful arts." Thus, Applicants assert that limiting the claims to recite a single immune response, such as a humoral response, provided merely by way of example in the application is unwarranted and would unduly restrict the scope of the subject matter for which protection is being sought.

Solely for the purposes of expediting prosecution of the instant application, Applicants have, however, amended independent claim 20 to indicate that the immune response is a humoral and/or cellular immune response. Claim 31 has been withdrawn without prejudice or disclaimer. Applicants submit that the amended claim set submitted herewith is in compliance with 35 U.S.C. 112 (first paragraph) and, therefore, respectfully request that this rejection be withdrawn.

35 U.S.C. 112, first paragraph (Written Description)

The Examiner rejected claims 20-31, 33-39 and 42, under 35 U.S.C. 112, first paragraph, alleging the claims fail to comply with the written description requirement. The Examiner stated that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner

alleged that the claims are drawn to an adjuvant comprising "a virus-like particle...derived from [PapMV]", yet the specification only discloses the entire PapMV coat protein as having an adjuvant effect and does not disclose any other PapMV proteins, or fragments of the coat protein, that are capable of enhancing an immunogenic response to antigen. The Examiner further alleged that the specification similarly fails to describe any regions or sequences within the coat protein that are responsible for immunogenicity and that the antigenicity of PapMV was new in the art such that the skilled artisan was unaware of the peptides that were capable of inducing an immune response. Thus, the Examiner alleged that, a skilled artisan could not reasonably conclude that Applicants were in possession of an antigenic PapMV peptide besides the entire coat protein as set forth in the specification.

Applicants respectfully traverse the Examiner's rejection for the following reasons. Firstly, Applicants assert that the instant application adequately describes various PapMV VLPs other than those comprising the entire PapMV coat protein. For example, at page 13, line 21 to page 14, line 1, the use of proteins, polypeptides, or parts thereof are described for production of the VLPs, as well as genetically modified versions of these proteins, such as deletions, insertions, and amino acid replacements. At page 13, lines 24-25, genetically modified versions of coat protein are specifically contemplated as one embodiment of the invention. Techniques for genetically modifying proteins, such as by deletion, insertion, and amino acid replacement, were well known to those skilled in the art at the date the present application was filed. As stated in the MPEP at §2163, "What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. See *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d at 1384, 231 USPQ at 94. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met."

Secondly, contrary to the Examiner's allegation, the instant specification, at page 14, lines 10 and 11, clearly teaches that it is **not** necessary for the viral portion of the fusion

protein to comprise a whole virus coat protein. In fact, as described in the instant specification, the inventors had recognised that the immunopotentiating property of the PapMV adjuvant lies in the repetitive structure of the PapMV (see, for example, page 9, lines 8-20). Thus, various forms of the coat protein, including fragments and genetically modified versions (as described at page 13, line 26 to page 14, line 1), can be used to produce the PapMV adjuvant, provided that the protein employed retains the ability to multimerize into a rod-like structure, *i.e.* a VLP (as described at page 9, line 22 and page 10, lines 4-15), which can be readily determined by standard techniques (see, for example, Example I, Example III (3rd paragraph) and Figure 3).

In this regard, Applicants also respectfully direct the Examiner's attention to the accompanying Inventor's Declaration at paragraph 11, which describes the construction of a VLP using a genetically modified version of the PapMV coat protein. This protein is capable of assembling into VLPs and potentiating an immune response, as shown in Exhibits I through III of the Inventor's Declaration.

Accordingly, Applicants assert that the instant application clearly and fully describes proteins suitable for use to provide the VLPs and the structural configuration required in order to achieve adjuvant immunogenicity and, as such, a worker skilled in the art having regard to the instant specification and art-known techniques for protein modification, would readily conclude that the inventor had possession of the claimed invention at the time the instant application was filed.

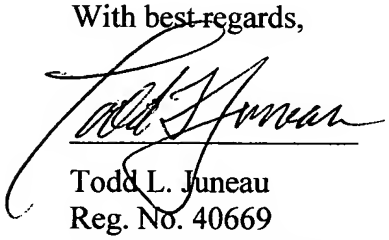
For the foregoing reasons, Applicants assert that the claims, currently on file, contain subject matter which is clearly and fully described in the specification. Solely for the purpose of expediting the prosecution of the instant application, however, Applicants have amended the claim set to more clearly define the subject matter for which protection is being sought. In particular, Applicants have amended independent claim 20 to specify that the VLP is derived from PapMV coat protein, and have amended claim 25 to indicate that the antigen is fused to a coat protein of the PapMV or VLP. Claim 26 has been

cancelled without prejudice or disclaimer. Applicants submit that the amended claim set submitted herewith complies with 35 U.S.C. 112, first paragraph, and, therefore, respectfully requests that this rejection be withdrawn.

Conclusion

All of the stated grounds for objection and rejection have been properly traversed, accommodated or rendered moot. Applicants, therefore, respectfully request that the Examiner reconsider all presently outstanding rejections and objections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided. Prompt and favourable consideration of this Amendment and Reply is respectfully requested.

With best regards,



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